UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,316	03/29/2004	Chandra U. Singh	AZAY:006US	1828

7590 09/28/2006

David L. Parker
Suite 2400
600 Congress Avenue
Austin, TX 78701

EXAMINER	
MAIER, LEIGH C	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/812,316	SINGH ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-30 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 4/3/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "*amorphous* cyclodextrin" in line 2. (emphasis added) There is insufficient antecedent basis for this limitation in the claim. The claim further states "the ration by weight of digitalis glycoside to amorphous cyclodextrin is 0.01 to 1." It is not clear if what is intended is (1) the ratio is exactly 0.01:1; or (2) the ratio can be within a range from 1:100 (*0.01*) to 1:1 (*1*). The latter appears to be more consistent with the description in the specification, but this is not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 13, 16, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones (US 4,555,504).

Jones discloses the preparation of inclusion complexes comprising a cyclodextrin (CD) and cardiac glycosides (CGs), digoxin and digitoxin. These complexes are isolated by lyophillization (freeze-drying). See examples 1, 2 and 6.

Claims 1-3, 7, 13, 20, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Pitha (US 4,727,064).

Pitha discloses the preparation of inclusion complexes comprising an amorphous CD and CGs, digoxin and oubain. The complexes are freeze-dried and compressed into tablets with a cellulose excipient. See abstract; Table 1; and examples 4-6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 13-19, 21, 22 and 24-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (US 4,555,504) in view of Michaels (US 4,182,330) with Conrad et al (US 5,380,716) to support inherency.

Jones exemplifies two species of cardiac glycosides complexed with a CD, as set forth above. The reference further teaches that CGs, generically, form complexes with CDs, affording a much greater solubility of these compounds. See col 1, lines 42-53. The reference teaches molar ratios (CD:CG) of 10:1 to 1:10. See col 2, lines 35-42. The weight ratios would be about 15:1 to 1:15 for digoxin and β–CD, for example. This may be administered in a variety of methods for the treatment of cardiac dysfunction. See col 2, lines 4-6 and col 3, lines 15-20. The reference does not teach the full range of CGs or the treatment of a specific proliferative disease.

Michaels teaches that CGs have utility for the treatment of cardiac dysfunction, such as congestive heart failure (CHF). The reference teaches the use of a wide variety of CGs, such as digitoxin, neriifolin, odoroside, oleandrin and proscillaridin, along with suggested dosages for treatment of cardiac disorders, such as CHF. See col 3, lines 2-47. This reference also notes that the low solubility of these compounds limits their use. See col 1, lines 31-35.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare cyclodextrin complexes with any known CG in order to increase their solubility and facilitate their use in the treatment of cardiac disorders, such as CHF. One of ordinary skill would reasonably expect success in preparing such complexes because their similarity in structure and because it was expressly suggested by Jones. Although not disclosed in these two references, CHF is known to be a proliferative disorder. See Conrad et al (US 5,380,716), for example at abstract. It would be within the scope of the artisan to prepare a

composition having a suitable concentration for the administration of a dosage suggested in the art through routine experimentation. It would be further within the scope of the artisan to administer the complex to the patient by any appropriate means.

Claims 1, 13-19 and 21-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (US 4,555,504) in view of Michaels (US 4,182,330) and further in view of Rubinfeld et al (US 5,824,668).

Jones and Michaels teach as set forth above.

Sterilization of a solution by filtration is well known in the art. Rubinfeld teaches specifically that a solution comprising a cyclodextrin complex may be sterilized by filtration through a 0.2 micron filter and generally discusses the importance of purity and sterility in pharmaceutical products. See col 11, lines 25-58.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize a solution comprising a solution comprising a CG/CD complex by filtration. Preparation of sterile solutions for distribution and administration to human subjects is the standard of care in the pharmaceutical industry. It would be within the scope of the artisan to select any method, such as filtration, with a reasonable expectation of success.

Claims 1-7, 13, 16, 21, 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (US 4,555,504) and Pitha (US 4,727,064).

Jones teaches as set forth above. The reference further teaches the inclusion of typical pharmaceutical additives, such as buffers, antioxidant, binders and preservatives. See col 3, lines 58-65.

Pitha teaches as set forth above. The reference specifically exemplifies the use of a polysaccharide as an excipient for the preparation of tablets.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare complexes comprising CGs and amorphous CDs for the increased solubility derived from the Pitha CDs. It would be the scope of the

Claims 1-11, 13, 16, 21, 22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones (US 4,555,504) and Pitha (US 4,727,064) and further in view of Stella et al (US 5,874,418).

Jones and Pitha teach as set forth. The combination of references does not teach the full scope of additives and excipients recited in the claims.

The recited additives and excipients are common and well known in the art. See, for example Stella at col 19-20.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the compositions that would be made obvious by the combination of Jones and Pitha as set forth above. In the absence of unexpected results, it would be within the scope of the artisan to further modify them by the addition of any common additives or excipients known in the art. The examiner finds no criticality in any recited excipient.

Claims 1-3, 5-8, 13-22 and 24-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braude et al (WO 00/47215) and Pitha (US 4,727,064).

Braude teaches the administration of CGs for the treatment of a variety of tumors. See abstract and pages 7-12. The reference further suggests these agents in combination with a variety of typical excipients, such as preservatives and buffers. See page 18. The reference further teaches dosages and methods of administration. See page 19.

Pitha teaches as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was known to modify the method of Braude—treatment of tumors with CGs—by preparing CD complexes, as taught by Pitha, to enhance their solubility. Pitha demonstrated the dramatically increased solubility of two particular CGs. Because of the similarity in structure, as demonstrated by Braude, one of ordinary skill would reasonably expect success in preparing such complexes of the recited compounds and administering them for the treatment of cancer, a proliferative disease. It would be within the scope to prepare compositions of an appropriate concentration for administration to a patient at the necessary dosage as determined by routine experimentation.

Claims 1-3, 5-8, 12-22 and 24-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braude et al (WO 00/47215) and Pitha (US 4,727,064) and further in view of either of (1) Sasaki et al (US 4,454,315); (2) Larm et al (US 4,707,471); (3) Williams et al (US 4,833,131); (4) Kanamaru et al (US 5,135,920) or (5) Raz et al (US 5,895,784).

Braude and Pitha teach as set forth above. The combination of references does not teach the use of the polysaccharides recited in claim 12.

The polysaccharides recited in claim 12 are all known for the use in the treatment of cancer. See, for example, (1) Sasaki at abstract; (2) Larm at col 4; (3) Williams at abstract; (4) Kanamaru at abstract or (5) Raz at abstract.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the composition made obvious by Braude and Pitha for the treatment of cancer. In the absence of unexpected results, it would be further obvious to combine any other agent known to be effective in treating cancer, such as those recited in claim 12, for the additive effects.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more. Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
September 20, 2006